

AORTIC REGURGITATION

Epidemiology

The prevalence of aortic regurgitation in the western world ranges from 0.1% in subjects 45-54 year-old to 2% in those ≥ 75 years.^{1,2}

Aetiology

Aortic regurgitation (AR) results from abnormalities of the aortic leaflets or the aortic root and annulus (Table 1). Degenerative and congenital conditions are the most prevalent causes of **chronic AR** in the western world, although no cause can be identified in certain occasions. Rheumatic heart disease is the most common cause worldwide.³ **Amphetamine** derivatives such as fefluramine, phentermine and benfluorex may account for up to 7% with regurgitant valve disease in general.⁴ The co-existence of severe conduction system abnormalities plus AR is associated with **HLA-B27**, an immunogenetic marker.⁵ Exposure to **fluoroquinolone** antibiotics has been associated with an increased risk of developing left-sided valvular regurgitation,⁶ but more recent data have refuted this possibility.⁷ **Acute AR** is most commonly caused by endocarditis, aortic dissection, ruptured fenestration of an aortic leaflet, chest trauma, or prosthetic valve dysfunction.⁸ Hypertension is associated with aortic root dilation and aortic valve disease.⁹ Bicuspid aortic valve is discussed in ACHD.

Pathophysiology and Natural History

Acute AR leads to rapid decompensation due to low forward cardiac output and pulmonary congestion. There is not time for compensatory LV dilation to occur and there is marked increase in end-diastolic pressure. Although there is some degree of compensation by the Frank-Starling mechanism, the ventricle is functioning on a steep pressure-volume curve because of the lack of chamber dilation. Thus, severe hypotension with a narrow pulse pressure occur rather than the systolic hypertension and widened pulse pressure that are characteristics of chronic severe AR. Mitral regurgitation in acute AR may occur either in diastole or in systole (when LVEDP exceeds LA pressure). Diastolic MR results in increased LA pressure and pulmonary oedema and is a specific indicator of acute severe AR.¹⁰

Chronic AR results in combined volume and pressure overload of the LV that is related to the severity of the regurgitant flow (Table 2). Systolic hypertension can contribute to progressive dilation of the aortic root and subsequent worsening of AR. In early, compensated severe AR, the LV adapts to the volume overload by eccentric hypertrophy with replication of sarcomeres in series and elongation of myofibers. Over time, progressive LV dilation and

systolic hypertension increase wall stress and the volume/mass ratio that eventually leads to overt LV systolic dysfunction. In decompensated severe AR, LV systolic dysfunction is accompanied by decreased LV diastolic compliance as a result of hypertrophy and fibrosis, leading to high filling pressures and heart failure symptoms. Asymptomatic patients with AR and normal LV function but LVESD > 50 mm develop LV dysfunction and symptoms and a risk of sudden death of 7-19% per year. Patients with chronic severe AR are at risk of developing irreversible left ventricular dysfunction before the onset of symptoms.¹¹ Asymptomatic patients with LV systolic dysfunction have a higher rate of events but the LV function may improve following AVR. Patients with moderate/severe mixed aortic valve disease have event rates comparable to patients with isolated severe aortic stenosis.¹²

Presentation

Acute AR is usually catastrophic and the patient may present in cardiogenic shock. In **chronic AR** exertional dyspnea is the most common manifestation, but angina can also occur because of a reduction in coronary flow reserve with predominantly systolic coronary flow.

Physical Examination

In **acute AR**, auscultation can be confusing due to the difficulty in distinguishing diastole from systole, and the diastolic murmur may be absent because of rapid equilibration of aortic and LV diastolic pressures. The only clue may be an **absent S2** in the setting of tachycardia, hypotension and pulmonary edema. S1 may be soft due to early MV closure that is an ominous prognostic sign calling for urgent surgery.

In **chronic AR** physical findings are related to increased stroke volume and widened blood pressure:

Bounding carotid pulse (**Corrigan's pulse**), head bobbing (**de Musset's sign**), pulsation of the uvula (**Muller's sign**), pistol shot sounds over the femoral artery with compression (**Traube's sign**), and capillary pulsations on the fingernail during compression with a glass slide (**Quincke's sign**) have been described with severe AR.

Diffuse, hyperdynamic **apical impulse** and perhaps **systolic thrill** may be present.

Soft or absent or paradoxically splitted **S2**

S3 may be present that does not necessarily indicates a failing LV.

Decrescendo diastolic murmur at the aortic area or the left sternal border with the patient leaning forward in expiration.

Mid-diastolic apical rumble (**Austin-Flint murmur**) possibly due to restriction of the MV opening by the high-pressure AR jet or to vibrations of the anterior mitral leaflet by a posteriorly directed AR jet.

Systolic ejection murmur due to high ejection volume.

Ejection click with BAV.

Investigations

ECG It may be normal or indicate LV hypertrophy. With early volume overload there may be prominent Q waves in leads I, aVL, and V3 to V6. With progressive disease the Q waves decrease but the total QRS amplitude increases.

Chest radiography It is usually normal. Cardiomegaly is a late feature in AS and calcification is a universal finding but rarely visible on chest X-ray. The proximal ascending aorta may be dilated, particularly in patients with bicuspid valves.

Echocardiography is the standard imaging procedure for assessment of the leaflets and the aortic root and quantitation of the severity of AR (Table 3 and Figure 1).¹³ M-mode echo may also be useful in demonstrating premature mitral valve closure. Doppler color flow mapping is used for quantification of AR. Vena contracta imaging and assessment of jet eccentricity are used, whereas PISA is less reliable than in MR. Volumetric LV measures and regurgitant fraction are superior to linear diameters in identifying patients at higher risk.¹⁴ In patients with mixed AS and AR, peak aortic jet velocity reflects both stenosis and regurgitation and represents a useful predictive parameter.¹⁵ Transesophageal echocardiography may be necessary for accurate assessment and particularly when dissection is suspected.

Computed tomography is useful for the assessment of aortic root dilatation.

Cardiac magnetic resonance is the most technique for LV volumes, EF and regurgitant fraction assessment.¹⁶

Cardiac catheterization is used when the CMR is not available or feasible and in cases with equivocal echo findings. Aortography allows visualization and quantification of the regurgitant jet. Grade 1 AR is contrast appearing in the LV but clearing with each beat. Grade 2 AR is faint opacification of the entire LV over several cardiac cycles. Grade 3 AR is opacification of the entire LV with the same intensity as in the aorta. Grade 4 AR is opacification of the entire LV on the first heart beat with an intensity higher than in the aorta. This method is subjective and depends on the amount of contrast injected and the size of the LV, particularly in significant AR.

Coronary angiography is necessary before surgery in patients with risk factors or clinical suspicion of coronary artery disease.

Therapy

Acute AR Vasodilation with sodium nitroprusside is used as a bridge to emergency surgery. Aortic balloon counterpulsation is absolutely contraindicated. Beta blockers prolong diastole and may worsen AR.

Chronic AR

Medical Therapy

Medical therapy is aimed at reducing systolic hypertension and thereby wall stress and improve LV function (Table 4). Two randomized studies have shown improvement of LV function with hydralazine and nifedipine, respectively.^{17, 18} Theoretically vasodilation with ACE/ARB should also be beneficial. Significant reduction of the regurgitant volume cannot be achieved with medical therapy because the regurgitant orifice area is fixed and the diastolic blood pressure already low. Thus, vasodilator therapy is recommended either in inoperable patients, or as bridge to surgery or in asymptomatic patients who have LV dilation but normal LVEF. Among patients with stage B AR, progression to stage C or D occurred in 21% during a median follow-up of 4.1 years. Baseline AR severity and the dimensions of the aortic valve annulus and sinotubular junction seem to be associated with progression, whereas systolic blood pressure is not.¹⁹

Surgical/Interventional Therapy

Surgery for AVR is indicated in patients with **severe AR and symptoms or signs of reduced LV function** (Tables 5 and 6, and Figures 2 and 3).^{20, 21} A detailed history for detection of symptoms is therefore essential.²² AVR should also be considered with progressive increases in LV volume or decreases in LVEF in serial studies. The threshold of LV dilatation for surgery may be lower in high-volume experienced centers (indexed LV end-systolic dimension ≥ 2 cm/m²).^{23, 24} Even among symptomatic patients with a severe reduction in LVEF (<35%), AVR results in improved survival rate.²⁰ Mortality rates for AVR are approximately 4.6% approaching 6% for AVR plus CABG. The 1-year permanent pacemaker implantation rate is 6.6% after AVR.²⁵ Repair of a tricuspid or bicuspid AV is also now a possibility.²⁶ The choice of a **mechanical or bioprosthetic** valve is discussed in detail in the Chapter on Prosthetic Valves. As with other valve diseases, optimum management of patients is hampered by the lack of definitive prospective clinical trials. In experienced centres, pure AR can generally be **repaired**, and optimal surgical treatment, especially in younger and selected patients, should aim to avoid aortic valve replacement and its related complications.²⁷ **TAVR** may also be an option in inoperable patients, but the possibility of requiring 2 valves and leaving residual aortic regurgitation remain important considerations.^{28, 29} Dedicated TAVR devices for AR have been developed.^{30, 31} Indications for combined valvular and coronary interventions are provided in General Principles.

Non-cardiac surgery

In symptomatic patients, If possible, intervention should be performed before noncardiac surgery (Table 7). In asymptomatic patients with moderate or greater degrees of AR and normal LV systolic function, elective noncardiac surgery can be performed. In patients with symptomatic severe AR or asymptomatic severe AR and LVESD >50 mm or LVESDi (LVESD/BSA) >5 mm/m² (in patients with small body size) or resting LVEF ≤50%, valve surgery is recommended prior to elective intermediate- or high-risk NCS. In patients with AR, if LV dysfunction is severe (EF <30%), non-cardiac surgery should only be performed if strictly necessary, after optimization of medical therapy for HF.

Exercise

Recommendations for exercise and participation in sports are provided in Table 9.

Pregnancy

The ACC/AHA 2020 GL on VHD recommend valve surgery during pregnancy in severe valve regurgitation and with NYHA class IV HF symptoms (Stage D) refractory to medical therapy (IIa-C-LD).

General recommendations are also provided in General Principles.

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